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PAPER

The effects of 2-week ingestion of (–)-hydroxycitrate and (–)-hydroxycitrate combined with medium-chain triglycerides on satiety, fat oxidation, energy expenditure and body weight

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OBJECTIVE: Assessment of the effect of 2-week supplementation with (–)-hydroxycitrate (HCA) and HCA combined with medium-chain triglycerides (MCT) on satiety, fat oxidation, energy expenditure (EE) and body weight (BW) loss.
DESIGN: Three intervention periods of 2 weeks separated by washout periods of 4 weeks. Double-blind, placebo-controlled, randomised and cross-over design.
SUBJECTS: Eleven overweight male subjects (mean ± s.d.; age, 47 ± 16 y; body mass index, 27.4 ± 8.2 kg/m^2).
INTERVENTION: Subjects consumed three self-selected meals and four iso-energetic (420 kJ) snacks daily with either no supplementation (PLA), 500 mg HCA (HCA) or 500 mg HCA and 3 g MCT (HCA + MCT). Each intervention ended with a 36 h stay in the respiration chamber.
RESULTS: There was a significant BW loss during the 2 weeks of intervention (PLA, −1.0 ± 0.4 kg, $P < 0.05$; HCA, −1.5 ± 0.5 kg, $P < 0.01$; HCA + MCT, −1.3 ± 0.2 kg, $P < 0.001$), but this reduction was not different between treatments. 24 h EE (PLA, 11.8 ± 0.2 MJ; HCA, 11.7 ± 0.1 MJ; HCA + MCT, 11.5 ± 0.1 MJ), 24 h RQ (0.85 ± 0.00 in all treatments) and the area under the curve of the appetite-related parameters were not different between treatments.
CONCLUSION: Two-week supplementation with HCA and HCA combined with MCT did not result in increased satiety, fat oxidation, 24 h EE or BW loss compared to PLA, in subjects losing BW.
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Keywords: (–)-hydroxycitrate; medium-chain triglycerides; satiety; energy expenditure; body weight loss

Introduction

The increasing incidence of obesity is a recognised medical problem in developed countries.[1] Obesity is the net result of disrupted balance between energy intake and energy output,[2] the excess being stored in the adipose tissue. It is a major factor for a number of diseases, including coronary heart diseases, hypertension, type 2 diabetes mellitus, pulmonary dysfunction, osteoarthritis and certain types of cancer.[3–5] Treatment of obesity is often unsuccessful. Weight loss can be achieved, but long-term weight maintenance after weight loss is rarely shown.[6–8] Therefore, identification of substances that improve or at least sustain satiety during energy restriction is needed. One possible way to improve satiety is to increase hepatic fatty acid oxidation. Evidence for a role of hepatic fatty acid oxidation in the control of eating has been shown in animals.[9] Therefore, finding ways to stimulate fatty acid oxidation in the liver should be promising for appetite and weight control. We hypothesise that stimulation of the post-ingestive fatty acid oxidation could modulate fat-induced satiety. We therefore investigated the potential of (–)-hydroxycitrate (HCA) and medium-chain triglycerides (MCT), which are believed to induce fatty acid oxidation,[10–17] to increase satiety and decrease body weight.

HCA is an active ingredient that is extracted from the rind of the fruit *Garcinia cambogia*, a native species to India, and is promoted as a weight loss agent. HCA is an inhibitor of ATP-citrate-lyase, a cytosolic (extramitochondrial) enzyme that catalyses the cleavage of citrate to oxaloacetate and acetyl-CoA.[17–19] HCA might induce satiety by inhibiting

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malonylCoA formation, which in turn would stimulate carnitine transferase activity, resulting in decreased fat synthesis and increased fat oxidation[20,21] or by increasing the rate of hepatic glycogen synthesis.[22] Furthermore HCA might promote weight maintenance by inhibiting or limiting de capacity for *de novo* lipogenesis,[18] especially along with a high carbohydrate diet. Up to now, however, the results on the effects of HCA on appetite, body weight and energy expenditure and its possible contribution as a weight loss agent in humans are controversial.[23–26] Several studies found a positive effect of HCA administration alone or in combination with other ingredients on appetite, energy intake, body weight loss, fat oxidation or energy expenditure,[27–31] but others did not.[32–35] To distinguish the satiety effect of HCA from the fatty acid oxidation effect, we conducted two separate studies. In our previous study we found no effect of HCA on satiety in subjects losing body weight.[36] In the present study, we concentrate on the possible effects of chronic HCA administration on fatty acid oxidation.

Medium-chain triglycerides (MCT) have been repeatedly suggested as a food ingredient that may contribute to the control of body weight. MCT are known to be rapidly hydrolysed and absorbed comparably to glucose.[37,38] Unlike long-chain triglycerides (LCT) that are transported in chylomicrons through the lymphatic system, MCT are converted into medium-chain fatty acids (MCFA) that directly enter the blood through the portal system. MCFA can cross the inner mitochondrial membrane in the liver and muscle independently of the acylcarnitine transferase system.[39] Studies showed that fatty acids delivered by MCT are preferentially oxidised and poorly stored within tissues, and that MCT have a marked thermic effect.[40] In addition to that, MCT have been shown to have satiating properties and to decrease food intake compared to LCT[13,15,41] by involving a cascade of pre-absorptive and post-absorptive mechanisms. However, the exact mechanism underlying the reduction in food intake after MCT ingestion is not fully understood.[57,42]

The aim of the present study was to investigate the effects of 2-week administration of HCA and HCA combined with MCT on satiety, fat oxidation, energy expenditure and body weight. We hypothesised that HCA supplementation might affect appetite and body weight regulation by increasing fat oxidation and metabolic rate, reflected by an increase in energy expenditure. We further hypothesised that the combination of HCA and MCT may have a stronger effect on fatty acid oxidation and consequently on satiety compared to HCA alone. In addition MCT could have a thermogenic effect.

Methods

Subjects

Eleven normal to moderately obese male subjects participated in this study. The subjects were recruited by advertisements in local newspapers. Selection took place following health criteria (no diabetes, no cardiovascular diseases, and no medical treatment) and body weight (BW) criteria (body mass index 25–31 kg/m^2). Baseline characteristics of the subjects are presented in Table 1. The subjects were not HCA or MCT users. The nature and risks of the experimental procedure were explained to the subjects, and all subjects gave their written informed consent. The study was approved by the Ethical Committee of Maastricht University.

Table 1 Subject characteristics at baseline

	Mean ± s.d.	*Range*
Age (y)	47 ± 16	27–56
Height (m)	1.77 ± 0.51	1.71–1.85
Weight (kg)	85.4 ± 25.8	73.4–98.6
Body mass index (kg/m^2)	27.4 ± 8.2	24.5–31.4
Waist circumference (cm)	94 ± 28	86–109
Hip circumference (cm)	102 ± 30	90–111
Waist–hip ratio	0.93 ± 0.27	0.83–1.04
Blood glucose (mmol/l)	5.21 ± 1.59	4.81–5.62
Blood triglycerides (mmol/l)	1.32 ± 0.70	0.44–2.05
F1 (cognitive restraint)	7 ± 4	2–15
F2 (disinhibition)	4 ± 3	1–8
F3 (hunger)	3 ± 2	0–6
Herman–Polivy restraint	16 ± 6	10–21

$n = 11$ men. F1–F3, *factors 1–3 of the Three Factor Eating Questionnaire.*

Experimental design

The experiment had a double-blind, placebo-controlled, randomised, cross-over design. The experimental design consisted of three intervention periods of 2 weeks separated by washout periods of 4 weeks. Each intervention period ended with a 36 h stay in the respiration chamber.

During the washout periods, the subjects consumed a self-selected and self-prepared diet. During the intervention periods, the subjects consumed at home three self-selected and self-prepared meals daily (breakfast, lunch, and dinner) with no restriction regarding type and amount of food. They were instructed to drink maximally one glass of alcoholic beverage per day. Between the meals, the subjects consumed an iso-energetic snack (cereal bar) of 22 g (energy, 420 kJ; protein, 0.7 g; fat, 4 g; carbohydrate, 14 g; dietary fibre, 0.5 g) with no supplementation (PLA), with supplementation of 500 mg (−)-hydroxycitrate (HCA; 850 mg SuperCitrimax HCA 600 SXG, HCA content 58, 81%, EuroChem Feinchemie GmbH, München, Germany) or 500 mg (−)-hydroxycitrate and 3 g medium-chain triglycerides (HCA + MCT). The dosage used was similar or higher to that used in other studies in which an effect of HCA on BW reduction was found (3 × 500 mg/day;[27,28] 2 × 55–110 mg/day[29]). The snacks were consumed at four fixed time points: 1 h before lunch, 2 h after lunch, 1 h before dinner and 2 h after dinner. Between the meals, the subjects were not allowed to eat with exception of the prescribed snacks. They were allowed to drink *ad libitum* water, coffee and tea (without sugar and milk). During the last 3 days of each intervention, the subjects were instructed to consume no alcohol and to eat

ad libitum food that was supplied from our laboratory for breakfast, lunch and dinner. The food had a food quotient (FQ) of 0.85.

Anthropometry

Body weight was measured during screening, at the beginning, after 1 week and at the end of each intervention period on a digital balance accurate to 0.02 kg (Chyo-MW-150K, Japan) with subjects in underwear, in the fasted state and after voiding their bladder. Height was measured to the nearest 0.1 cm during screening using a wall-mounted stadiometer (Seca, model 220, Hamburg, Germany). The body mass index was calculated by BW/height^2 (kg/m^2).

The distribution of fat was investigated during screening by measuring the waist and hip circumferences and calculation of the waist–hip ratio (WHR). The waist circumference was measured at the site of the smallest circumference between the rib cage and the ileac crest, with the subjects in standing position. The hip circumference was measured at the site of the largest circumference between the waist and the thighs. The WHR was calculated by dividing the waist circumference by the hip circumference.

Body composition was measured at the beginning and at the end of each intervention period by hydrodensitometry and deuterium (^2H_2O) dilution technique[43] and was calculated using the combined equation of Siri.[44] Body weight was measured in the fasted state with a digital balance accurate to 0.01 kg (Sauter Typ E1200, Ebingen, Germany). Whole body density was determined by underwater weighing with simultaneous assessment of long volume residual with the helium dilution technique using a spirometer (Volugraph 2000, Mijnhardt, The Netherlands). Measurements were performed in triplicate and the average was used to calculate body density. The dilution of the deuterium isotope is a measure for total body water (TBW).[45] Subjects were asked to collect a urine sample in the evening just before drinking a weighed amount of deuterium enriched water solution. After ingestion of the deuterium solution no further fluid or food consumption was permitted. Ten hours after ingestion of the deuterium solution a second urine sample (second voiding) was collected. Deuterium concentration in the urine samples was measured using an isotope ratio mass spectrometer (Micromass Optima, Manchester, UK). TBW was obtained by dividing the measured deuterium dilution space by 1.04.[43] Fat-free mass (FFM) was calculated by dividing the TBW by the hydration factor 0.73. By subtracting FFM from BW, fat mass was obtained. Fat mass expressed as a percentage of BW revealed body fat percentage.

Eating behaviour

Eating behaviour was analysed during screening, during the first and the last day of each intervention period using a validated Dutch translation of the Three Factor Eating Questionnaire (TFEQ).[46,47] Cognitive restrained and unrestrained eating behaviour (factor 1), emotional eating and disinhibition (factor 2) and the subjective feeling of hunger (factor 3) were scored. Body weight concern and chronic dieting behaviour were investigated with the Herman Polivy questionnaire (HP).[48]

Blood parameters

At the beginning and at the end of each intervention period, a fasting blood sample of 10 ml was obtained and mixed with EDTA to prevent clotting. Plasma was obtained by centrifugation (4°C, 3000 rpm, 10 min) and stored at −80°C until analysis of glucose by a hexokinase method (Roche Diagnostics, Hoffmann-La Roche, Basel, Switzerland), triglycerides (GPO-trinder 337, Sigma), free fatty acids by an ACS-ACOD method (Wako chemicals, Neuss, Germany), glycerol by a glycerolkinase-lipase method (Boehringer, Mannheim, Germany), β-hydroxybutyrate (BHB) by the method of Moore *et al*[49] using a semi-automated centrifugal spectrophotometer (Cobas Fara, Roche Diagnostics), and insulin with ELISA (Mercodia 10-1113-01).

Daily energy intake

Energy intake over the previous week was recorded at the beginning and at the end of each intervention period using a food frequency questionnaire. Personal instruction was given in advance. The food frequency questionnaires were analysed using the Dutch food composition table[50] and the accessory computer program (Becel Nutrition Program 1988).

Daily energy intake before intervention and during the second week of intervention was compared with predicted 24 h energy expenditure[51] that amounted on average 12.0 ± 1.1 MJ/day. Since predicted 24 h energy expenditure was significantly higher compared to the reported energy intakes (before intervention: PLA, 6.9 ± 0.4 MJ/day; HCA, 6.5 ± 0.4 MJ/day; HCA + MCT, 7.1 ± 0.5 MJ/day; during the second week of intervention: PLA, 7.5 ± 0.5 MJ/day; HCA, 7.9 ± 0.3 MJ/ day; HCA + MCT, 8.6 ± 0.5 MJ/day) and mean changes in reported energy intake were not related to mean changes in body weight ($r = 0.04$; $P > 0.05$), these data were not used for further analysis.

Mood

Changes in mood during intervention were scored on anchored 100 mm visual analogue scales at the beginning and at the end of each intervention period.[52]

Tolerance

Tolerance of the snacks was determined at the end of each intervention period using a questionnaire on occurrence of gastrointestinal and other complaints and scored on a 5

points scale (0 = not at all, 1 = less, 2 = sometimes, 3 = relatively much, 4 = very much).

Indirect calorimetry

Oxygen consumption and carbon dioxide production were measured in a whole room calorimeter.[53] The respiration chamber was a 14 m^3 room, furnished with a bed, chair, computer, television, radio-cassette player, telephone, intercom, sink and toilet. The room was ventilated with fresh air at a rate of 70–80 l/min. The ventilation rate was measured with a dry gas meter (Schlumberger, type 4, the Netherlands). The concentration of oxygen and carbon dioxide was measured using a paramagnetic O_2 analyser (Hartmann & Braun, type Magnos 6G, Germany; Servomex, type OA184A, UK) and an infrared CO_2 analyser (Hartmann and Braun, type Uras 3G, Germany). During each 15 min period, six samples of outgoing air for each chamber, one sample each of fresh air, zero gas and calibration gas were measured. The gas samples to be measured were selected by a computer that also stored and processed the data.[53]

Physical activity

In the respiration chamber subjects followed a protocol consisting of fixed times for breakfast, lunch and dinner, sedentary activities and bench stepping exercise. The bench stepping exercise was performed three times a day (10:30 h, 14:30 h, and 20:30 h) for 30 min at intervals of 5 min exercise alternated with 5 min rest, at a rate of one step per second with a bench height of 25 cm. Apart from the exercise protocols, subjects were not restricted in their activities, only sleeping and strenuous physical activity were not allowed. Physical activity was monitored using a radar system working on the Doppler principle.

Energy intake

Before entering the respiration chamber, the subjects consumed *ad libitum* a standardised dinner (pasta meal; energy, 393 kJ/100 g; protein, 3.8 g/100 g; carbohydrate, 11.1 g/100 g; fat, 3.8 g/100 g) and food intake was determined.

Energy intake (EI), adapted to reach energy balance, was determined from 24 h sleeping metabolic rate (SMR) measured during the first night and multiplied by an activity index of 1.6.[54] The subjects received a diet divided over three meals (breakfast at 08:30 h, lunch at 12:00 h and dinner at 18:00 h) and four snacks (1 h before and 2 h after lunch, 1 h before and 2 h after dinner). The food had a FQ of 0.85.

Energy expenditure and substrate oxidation

Twenty four hour energy expenditure (24 h EE) consisted of sleeping metabolic rate (SMR), diet-induced thermogenesis (DIT) and activity-induced energy expenditure (AEE). Twenty four hour EE and 24 h respiratory quotient (RQ) were calculated from 07:00 h to 07:00 h, from oxygen consumption and carbon dioxide production according to the method of Weir.[55] SMR was measured on both nights and was defined as the lowest mean EE measured over three consecutive hours between 00:00 h and 07:00 h. The average SMR of the two nights was used in further calculations. DIT was calculated by plotting EE against radar output, both averaged over 30 min periods. The intercept of the regression line at the lowest radar output represented the energy expenditure in the inactive state (resting metabolic rate, RMR), consisting of SMR and DIT.[56] DIT was determined by subtracting SMR from RMR. AEE was determined by subtracting RMR from 24 h EE. Carbohydrate, fat and protein oxidation was calculated using oxygen consumption and carbon dioxide production and urinary nitrogen excretion:[57]

$$\text{Protein oxidation (g/day)} = 6.25 \times N$$

$$\text{Fat oxidation (g/day)} = 1.718 \times VO_2 - 1.718 \times VCO_2 - 0.315 \times P$$

$$\text{Carbohydrate oxidation (g/day)} = 4.17 \times VCO_2 - 2.965 \times VO_2 - 0.390 \times P$$

where N is total nitrogen excreted in urine (g/day); VO_2 is oxygen consumption (l/day); VCO_2 is carbon dioxide production (l/day); P is protein oxidation (g/day).

Twenty-four hour urine was collected from the second voiding on the day of the experiment until the first voiding of the following day. Samples were collected in containers with 10 ml H_2SO_4 to prevent nitrogen loss through evaporation. Volume and nitrogen concentration were measured, the latter using a nitrogen analyser (Elemental Analyzer, CHN-O-Rapid, Heraeus).

Satiety

During the stay in the respiration chamber, appetite ratings (hunger, satiety, fullness, desire to eat, appetite, anticipated food intake and thirst) were scored on anchored 100 mm visual analogue scales.[47] Questionnaires were completed at 10 fixed time points, respectively immediately before and after breakfast, in the morning at 10:30 h, immediately before and after lunch, in the afternoon at 15:00 h, immediately before and after dinner, in the evening at 20:30 h, and before sleeping at 23:30 h. Appetite ratings during 24 h stay in the respiration chamber were expressed as area under the curve (24 h AUC), corrected for the subject's minimum score.

Statistical analysis

Data are presented as mean ± standard error (s.e.). Differences between the treatments were determined by analysis of variance for repeated measures (ANOVA) and Sheffe-F *post hoc* test (Statview SE Graphics™). The measurements at the beginning and at the end of the experiment were compared using paired *t*-tests. Pearson correlation coefficients, *r*, were

calculated to determine the relationship between selected variables. The level of significance was set at $P < 0.05$.

Results

There was a significant BW reduction during 2 weeks of intervention (PLA, -1.0 ± 0.4 kg, $P < 0.05$; HCA, -1.5 ± 0.5 kg, $P < 0.01$; HCA + MCT, -1.3 ± 0.2 kg, $P < 0.001$). However, BW reduction was not different between treatments. BW loss was greater during the first compared to the third intervention period (-2.0 ± 0.5 kg *vs* -0.5 ± 0.2 kg; $P < 0.05$) with values for the second intervention intermediate (-1.3 ± 0.3 kg). Body fat decreased with HCA + MCT ($-0.9 \pm 0.4\%$, $P < 0.05$), but not with PLA and HCA ($-0.6 \pm 0.8\%$ and $-0.3 \pm 0.3\%$, respectively). However, no difference in body fat loss was found between treatments.

Scores on the HP and the TFEQ questionnaires were similar for all treatments and did not change during intervention.

Fasting plasma glucose concentration before and after intervention was similar for each treatment. Plasma glucose concentration was reduced as a result of intervention with PLA (-0.17 ± 0.07 mmol/l; $P < 0.05$), but not with HCA and HCA + MCT (-0.09 ± 0.09 and -0.08 ± 0.09 mmol/l, respectively). However, reduction in plasma glucose was not different between treatments. Fasting plasma FFA, glycerol, triglycerides and insulin concentrations before and after intervention as well as changes during intervention were similar between treatments. Fasting plasma BHB before intervention was higher with HCA + MCT compared to PLA ($P < 0.05$). There was no difference in plasma BHB after intervention or in plasma BHB change during intervention between treatments.

There was no change in mood (relaxed, gloomy, pleasant, angry, afraid, sad) during intervention, and no differences were found between treatments. The snacks were similarly tolerated in all treatments and values for complaints remained low. Compliance to the snacks was determined by asking the subjects how many snacks were left. A mean of 96% of the snacks was consumed, indicating a high compliance to the snacks. Food intake during *ad libitum* meal before entering the respiration chamber was similar for all treatments (PLA, 2153 ± 102 kJ; HCA, 2076 ± 161 kJ; HCA + MCT, 2234 ± 140 kJ).

Mean 24 h EI and 24 h EE during the stay in the respiration chamber are presented in Figure 1. EI was chosen to reach energy balance. However, the subjects tended to be in negative energy balance (PLA, -0.6 ± 0.3 MJ; HCA, -0.5 ± 0.2 MJ; HCA ± MCT, -0.5 ± 0.3 MJ; all $P < 0.1$), but the level of negative energy balance was not different between treatments. There was no difference in SMR, RMR, DIT and AEE between treatments (Figure 1). DIT was $7.7 \pm 1.3\%$, $8.9 \pm 3.2\%$ and $7.7 \pm 1.3\%$ of EI with PLA, HCA and HCA + MCT, respectively (NS). Calculated physical activity index, defined as EE divided by SMR, was not different between treatments (PLA, 1.65 ± 0.03; HCA, 1.62 ± 0.02; HCA + MCT, 1.61 ± 0.02).

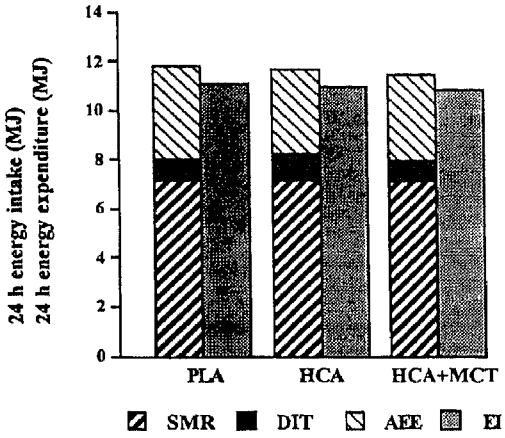

Figure 1 Twenty four hour energy intake and 24 h energy expenditure. Values are means. PLA = placebo; HCA = (−)-hydroxycitrate, MCT = medium-chain triglycerides; SMR = sleeping metabolic rate; DIT = diet-induced thermogenesis; AEE = activity-induced energy expenditure; EI = energy intake. Statistical significance was determined by an analysis of variance for repeated measures (ANOVA).

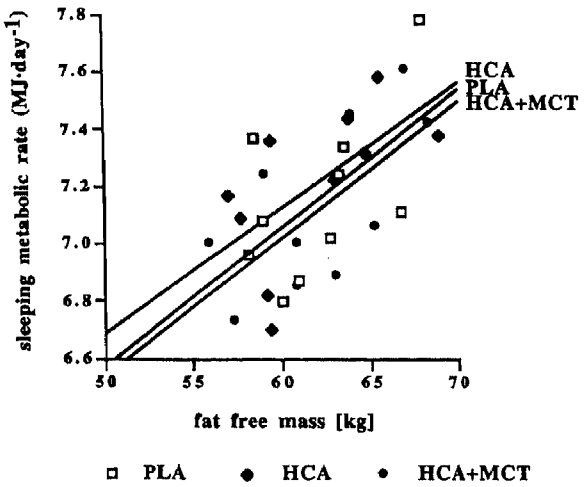

Figure 2 Relation between sleeping metabolic rate and fat-free mass. PLA = placebo; HCA = (−)-hydroxycitrate; MCT = medium-chain triglycerides. Relationship between variables was determined by calculating Pearson correlation coefficients. PLA, $r = 0.57$, $P < 0.1$; HCA, $r = 0.62$, $P < 0.1$; HCA + MCT, $r = 0.67$, $P < 0.05$.

SMR was related to FFM with HCA + MCT ($r = 0.67$, $P < 0.05$), and tended to be related to FFM with PLA and HCA ($r = 0.57$ and $r = 0.62$, respectively; $P < 0.1$; Figure 2). 24 h EE was not related to FFM in any of the treatments (PLA, $r = 0.34$; HCA, $r = 0.52$; HCA + MCT, $r = 0.45$; $P > 0.05$). There was no difference in protein (PLA, 82 ± 4 g/day; HCA, 81 ± 3 g/day; HCA + MCT, 74 ± 4 g/ day), fat (PLA, 80 ± 4 g/day; HCA, 81 ± 6 g/day; HCA + MCT, 77 ± 3 g/day) and carbohydrate oxidation (PLA, 201 ± 7 g/day; HCA, 192 ± 9 g/day;

HCA + MCT, 202 ± 7 g/day) between trials. Twenty-four hour RQ and non-protein RQ were similar in all trials (PLA, 0.85 ± 0.00 and 0.85 ± 0.00; HCA, 0.85 ± 0.00 and 0.84 ± 0.01; HCA + MCT, 0.85 ± 0.00 and 0.85 ± 0.00, respectively).

The 24 h AUC of hunger, satiety, fullness, desire to eat, appetite, anticipated food intake and thirst were similar in all treatments. Satiety was higher with HCA compared to HCA + MCT before dinner and fullness was higher with PLA compared to HCA before sleeping ($P < 0.05$). The subjects felt thirstier with PLA compared to HCA after dinner ($P < 0.05$). There was no difference at any time point in hunger, desire to eat, appetite, and anticipated food intake between treatments.

Discussion

In the present study, the potential of HCA and HCA combined with MCT on satiety, fat oxidation, energy expenditure and body weight was investigated in overweight men. The results did not support the hypothesis that HCA supplementation may be effective on appetite and weight control by increasing fat oxidation, and that MCT may have an additional effect.

Results on the effect of HCA supplementation in humans are controversial. Several studies found a positive effect of HCA alone or in combination with other ingredients, (eg chromium, caffeine, chitosan) on appetite,[22,30] 24 h energy intake[31] and body weight loss.[21–30] However, other studies did not find a significant effect of HCA on body weight.[32,35] HCA has been suggested to contribute to body weight loss by increasing fat oxidation and inducing satiety. Until now, few studies have investigated the effects of HCA ingestion on fat oxidation and energy expenditure in humans. Kriketos *et al*[33] found no effect of 3 days HCA supplementation (3.0 g/day) on fat oxidation and energy expenditure during rest or moderate exercise in sedentary humans. Similarly, van Loon *et al*[34] found no acute effect of HCA on energy expenditure and fat oxidation during rest and exercise in trained subjects, even following ingestion of large quantities of HCA (18.3 g). From these results, it may be argued that treatment with HCA was not sufficiently long and that HCA might have an effect on fat oxidation or other parameters such as appetite only over a longer investigation period. In the present study, supplementation with HCA and HCA combined with MCT lasted 2 weeks. However, no effect of HCA on fat oxidation or 24 h energy expenditure was found, and MCT did not result in an additional effect.

HCA administration has been shown to inhibit the rate of lipogenesis in rodents[18,58,59] and to increase the rate of hepatic glycogen synthesis,[22] but this has not been confirmed in humans. An excess energy intake as carbohydrate is needed to promote *de novo* lipogenesis and to increase glycogen synthesis. However, the subjects who participated in the present study were in a state of negative energy balance. This is confirmed by a body weight loss > 1 kg during the two weeks of intervention. Body weight loss resulted from a food intake regimen that prescribed to refrain from food consumption in between meals, with exception of the four snacks and non-caloric beverages, and to minimise alcohol intake. This negative energy balance may explain why HCA was not effective in reducing appetite and inhibiting fat synthesis as the conversion of citrate into acetylCoA by ATP-citrate-lyase only occurs when energy intake exceeds the energy requirements of the body. In other words, when a low-energy diet did not meet the energy requirements of the body, carbohydrate will be used in the citric acid cycle to produce ATP for energy rather than to form citrate, the substrate for *de novo* fatty acid synthesis. The results suggest that HCA is not effective in inhibiting fat synthesis or stimulating hepatic glycogen formation in a condition of a moderate negative energy balance. The ineffectiveness of HCA in dieting humans in fact has also been observed in other studies.[32,50] Moreover, in a condition of energy balance, Westerterp-Plantenga and Kovacs[31] found that administration of HCA for two weeks resulted in reduced 24 h energy intake on a subsequent test day.

In conclusion, it has been shown that, in circumstances when two mechanisms which may play a role in the effectiveness of HCA (ie *de novo* lipogenesis, hepatic glycogen synthesis) are very likely excluded, the other mechanism (ie fatty acid oxidation), which also might induce satiety, was not present. If HCA is an effective food supplement in relation to body weight regulation, it would probably be effective by inhibiting *de novo* lipogenesis or by stimulating hepatic glycogen synthesis. HCA may not be effective in inhibiting *de novo* lipogenesis and stimulating hepatic glycogen formation in a condition of negative energy balance and body weight loss. HCA might therefore be effective in prevention of weight (re)gain, and thus in prevention of obesity, rather than in supporting body weight loss. Further confirmation needs to be obtained from experiments on possible effects of HCA on *de novo* lipogenesis and glycogen synthesis during weight (re)gain in humans.

Supplementation with MCT did not result in an additional effect on satiety, 24 h energy intake, fat oxidation or body weight. Studies showed that MCT have satiating properties and decrease food intake compared to LCT.[13,15,41] Van Wymelbeke *et al*[41] found that a breakfast supplemented with MCT (ca 43 g) decreased energy intake during a free-choice lunch. Rolls *et al*[13] found that a small preload of MCT (*ca* 18 g, 36 g or 54 g) incorporated into a liquid meal was more effective at suppressing energy intake of a subsequent meal presented 30 min later, compared to LCT, already with the lowest dosage. In the present study, a lower dosage of MCT (12 g/day) was used. This might explain why no effect of MCT was found on energy intake. Studies also showed that MCT increases thermogenesis and fat oxidation.[40] The stimulating effect of MCT on energy expenditure was shown with low dosages of MCT (15 and 30 g/day) but disappeared at a dosage below 15 g/day.[60] This may indicate that the dosage of MCT used in the present study was to low in order to find an effect on energy expenditure. Finally, we are not able to make statements about the efficacy of MCT

themselves, as they were not investigated alone. Since HCA was not effective in this study, it is possible that the possible effect of MCT was inhibited.

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